DIARECT Newsletter

Summary

Dear Madam or Sir,

The AACC Annual Scientific Meeting and Clinical Lab Expo is the world's premier gathering for laboratory medicine. This year 20,000 laboratory scientists from a broad range of specialties are expected to attend. You will have the opportunity to connect with global leaders in clinical chemistry, molecular diagnostics, mass spectrometry, translational medicine, lab management and buyers of your *in vitro* diagnostic products. With more than 200 educational and scientific sessions, you keep pace with changes in the field.

The 70th AACC Annual Scientific Meeting and Clinical Lab Expo will take place in Chicago from July 29 – August 2, 2018. To learn more about the event click here.

DIARECT will be attending and would like to invite you to stop by our booth **#3035**. It is our pleasure to meet up with business partners, customers and potential new clients.

This issue of our Newsletter gives you a first impression and description of the newest additions to DIARECT's extensive product portfolio. To get an overview of all our products, including the antigens to be presented at this year's AACC, have a look at our new product list, available at this link: product list

If you wish to personally meet with a member of the DIARECT team at the Clinical Lab Expo or are interested in receiving more information, please feel free to contact us at:

Email info@diarect.com
Tel. +49 761 47979-0

We are looking forward to seeing you in Chicago!

DIARECT AG

Completing the *Anaplasma* portfolio: *Anaplasma phagocytophilum* OmpA

Human Granulocytic Anaplasmosis (HGA) was first recognized in the United States and is the most common tick-borne disease after Borreliosis. It is endemic in 42 countries with an overall case fatality of 5%. The causative agent of HGA is the rickettsial species *Anaplasma phagocytophilum*, a Gram-negative obligate intracellular pathogen infecting mammalian hosts worldwide. It invades and replicates within neutrophils by employing an array of mechanisms to subvert their bactericidal activity. Characteristic is the development of intracytoplasmic morulae within those peripheral blood granulocytes. Several epitopes on surface proteins of *Anaplasma phagocytophilum* are targeted during an immune response.

Major outer membrane protein A (OmpA) of *A. phagocytophilum* is a peptidoglycan-binding lipoprotein, transcriptionally upregulated during tick transmission feeding and playing an important role in the pathogenesis of HGA. The integral outer membrane channel belongs to the porin superfamily, which share a beta-barrel structure.

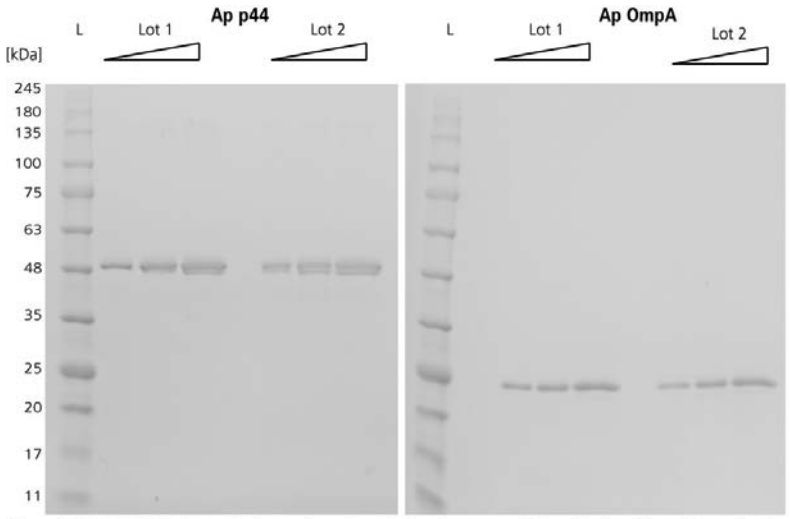

Figure 1: SDS-PAGE of two independent lots of *A. phagocytophilum* (Ap) p44 and OmpA. The molecular weight of protein standards included in the size ladder (L) are indicated on the left.

The invasion domain of OmpA is conserved in all *Anaplasma* and *Ehrlichia* species. Invasion is mediated by interaction of the protein with α2,3-sialic acid of the sialyl Lewis x (sLex) tetrasaccharide, which caps P-selectin glycoprotein ligand-1 (PSGL-1) and other glycoproteins on eukaryotic cell surfaces. Binding of the bacterium to these receptors on the membrane promotes endocytosis. Therefore, the invasin OmpA, together with other proteins, is important for entry into mammalian cells and critical for infection of neutrophils in host cells. Using an agonist for OmpA receptors, e.g. glutathione S-transferase (GST)–OmpA, shows that *A. phagocytophilum* infection of host cells is reduced by approximately 50 % as it blocks access of native OmpA on the bacterial surface to sialic acids.

Until now, DIARECT has provided the immunodominant major surface protein 5 (Msp5), also present in the salivary glands of infected ticks, and *A. phagocytophilum* p44, a transmembrane protein of the outer membrane, which is thought to enable the bacterium to avoid host immune surveillance. To complete the *Anaplasma* product line, DIARECT is now offering a third *A. phagocytophilum* antigen produced in *E.coli* to expand this product line: OmpA. All three proteins are considered main antigens of antibody response to HGA.

Catalog No.	Product name
45600 / 45601	*Anaplasma phagocytophilum* Msp5
45800 / 45801	*Anaplasma phagocytophilum* OmpA NEW!
45500 / 45501	*Anaplasma phagocytophilum* p44

References:
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Kahlon et al. (2013) Infect Immun. 81:65-79
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Ojogun et al. (2012) Infect Immun. 80: 3748–3760
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Park et al. (2003) Infect Immun. 71: 4018–4025
Rikihisa et al. (2007) Journal Bacteriol. 189: 7819–7828
Wang et al. (2013) PLoS One. 8 (10): e78189

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Tel: +49 761 47979-0
Email: info@diarect.com

New Humanized Monoclonal Antibodies: PCNA humAb IgG and Mi-2 humAb IgG

The nucleosome remodeling deacetylase (NuRD) complex exerts histone deacetylase activity and functions in the regulation of gene transcription. Mi-2 protein, a subunit of the NuRD complex, is a DNA-dependent ATPase helicase and appears to be involved in the repair of the basal epidermis.

Mi-2 autoantibodies are considered specific serological markers of dermatomyositis, an idiopathic myopathy characterized by the presence of inflammatory infiltrates within skeletal muscle. Together with adult polymyositis, dermatomyositis is one of the most common subtypes of these idiopathic myopathies along with inclusion body myositis, childhood myositis, malignancy-associated myositis, and myositis in overlap with mixed connective tissue disease.

Detected in about 20% of myositis sera, anti-Mi-2 autoantibodies are proven markers for acute onset, good prognosis and good response to therapy.

Proliferating cell nuclear antigen (PCNA; syn. Cyclin), a co-factor of DNA polymerase delta, forms homotrimers around double stranded DNA, and is involved in DNA replication and repair. Since its expression rate correlates with the rate of DNA replication, PCNA is a proliferation marker in basic research.

Systemic lupus erythematosus (SLE) is a debilitating, chronic, life-threatening, systemic autoimmune disease that can affect virtually any organ. The course of SLE varies from mild episodic illness to a fatally severe disease.
PCNA autoantibodies have been reported to be serological markers of SLE, together with other antibodies, and recognize specific conformational epitopes. In particular they are present in those patients suffering from arthritis and hypocomplementemia, and drop below detection limits following drug treatment.

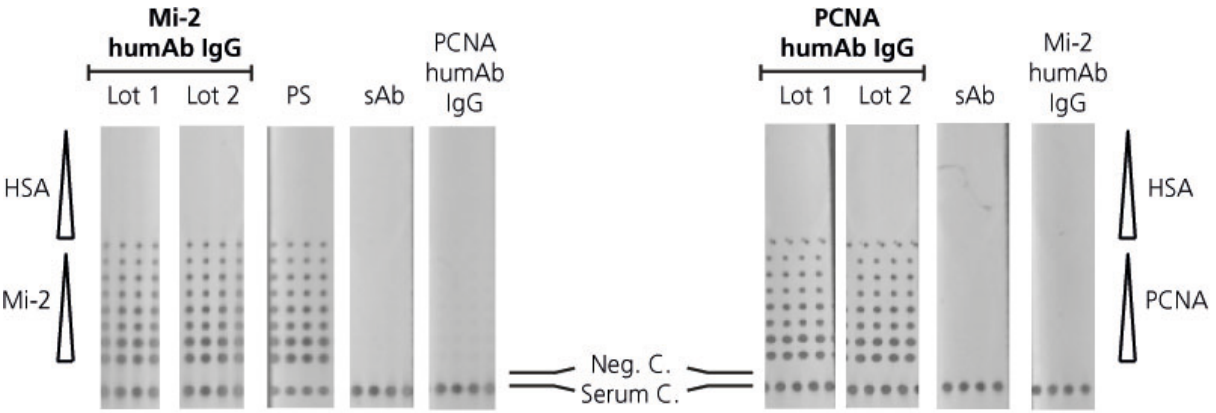

Figure: Immunodot analyses using anti-Mi-2 (left) and anti-PCNA (right) human chimeric IgG antibodies, two lots each, showing reactivity with patient sample (PS) and the respective recombinant antigens Mi-2 and PCNA. Increasing amounts of protein and HSA control were printetd on nitrocellulose membranes as indicated. Negative buffer control and serum control were printed on the bottom of the membranes. As negative antibody-controls secondary antibody only and an alternative antibody not matching the antigen was used (PCNA humAb IgG or Mi-2 humAb IgG, respectively).

Immunoassays for the detection of antibodies in patient samples require reference material to determine cut-off values and test assay integrity, and these are then included in the kit as calibrators or positive controls. One of the latest advances in assay development are chimeric monoclonal antibodies as an alternative to characterized disease state plasma, which are limited in availability, show variability, and there are also safety and ethical issues. Two years ago, DIARECT introduced the first human chimeric monoclonal antibodies of this new product line.

These antibodies are produced in transgenic mouse strains in which the sequence for mouse IgG1 Fc region is substituted with the human sequence. After mouse immunization and hybridoma technology, antibodies are generated that retain a human constant region required for recognition by the anti-human conjugate.

DIARECT currently provides tissue-specific chimeric antibodies for the detection and diagnosis of autoimmune liver diseases and SRP54 humAb IgG for myositis. DIARECT is further expanding this product line with the introduction of Mi-2 humAb IgG and PCNA humAb IgG. Additional new products related to autoimmune liver and systemic autoimmune diseases will follow shortly.

Catalog No.	Product name
36700	Mi-2 humAb IgG NEW!
36600	PCNA humAb IgG NEW!
36500	SRP54 humAb IgG
36100 / 36101	LC1 humAb IgG
36400 / 36401	LKM1 humAb IgG
36300 / 36301	PDC-E2 humAb IgG

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Heinlen et al. (2010) PloS One. 10:e9599
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Miyachi et al. (1978) J Immunol. 121:2228-2234
Sherer et al. (2004) Semin Arthritis Rheum. 34:501-537

For questions or additional information please feel free to contact us at:
Tel: +49 761 47979-0
Email: info@diarect.com

Distributors

To facilitate the world-wide sales of our antigens, DIARECT has distribution agreements with select companies.

If you are located in North America, DIARECT's products are exclusively distributed by:

SurModics IVD, Inc.
9924 West 74th Street
Eden Prairie, MN 55344
USA
Phone +1 952 500 7200
Toll-free +1 800 755 7793
Fax +1 952 500 7201
orders@surmodics.com
www.surmodics.com

If you are located in China, DIARECT's products are distributed by:

Shanghai BioSun Sci&Tech Co., Ltd.
Room K, 5F, Bldg. No.1
825 Zhaojiabang Road
Shanghai 200032
P.R. China
Phone +86 21 54253791
Fax +86 21 64280007
biosun@biosun.cn
www.biosun.cn